SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. General Information

Device Generic Name: Iliac Stent

Device Trade Name: Zilver® Vascular Stent

Applicant's Name and Address: Cook Incorporated
750 Daniels Way
Bloomington, IN 47404

Premarket Approval (PMA) Application Number: P050017

Date of Panel Recommendation: None

Date of Notice of Approval to Applicant: June 26, 2006

II. Indications for Use

The Zilver® Vascular Stent is intended for use as an adjunct to percutaneous transluminal angioplasty (PTA) in the treatment of symptomatic vascular disease of the iliac arteries up to 100 mm in length, with a reference vessel diameter of 5 to 9 mm. Patients should be suitable candidates for PTA and/or stent treatment.

III. Contraindications

There are no contraindications known at this time based on the clinical data.

IV. Warnings and Precautions

The warnings and precautions can be found in the labeling for the Zilver® Vascular Stent

V. Device Description

The Zilver® Vascular Stent is a self-expanding stent made from nitinol. It is a flexible slotted-tube that is designed to provide support and flexibility in the vessel upon deployment. Post-deployment, the stent is designed to impart an outward radial force upon the inner lumen of the vessel, establishing patency in the stented region. The Zilver® Vascular Stents are preloaded in 5, 6, and 7 Fr delivery systems. Table 1 shows the available diameters and lengths of the 5, 6, and 7 Fr Zilver® Vascular Stents.

Table 1. Diameters and Lengths of 5, 6, and 7 Fr Zilver® Vascular Stents and Delivery Systems

	Zilver® Vascular Stents and Delivery Systems														
	5 Fr					6 Fr					7 Fr				
	Stent Lengths (mm)														
Stent Outer Diameter (mm)	20	30	40	60	80	20	30	40	60	80	20	30	40	60	80
6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
7	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
8	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
9	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
10	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

VI. Alternative Practices and Procedures

Alternative procedures to treat symptomatic vascular disease of the iliac arteries include percutaneous transluminal angioplasty alone, percutaneous transluminal angioplasty accompanied by stenting, thrombolytic therapy, conservative medical management, or surgical procedures.

VII. Marketing History

The Zilver® Vascular Stent has been marketed for vascular use in the following countries: Algeria, Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, China, Columbia, Czech Republic, Denmark, El Salvador, Estonia, Finland, France, Germany, Greece, Guatemala, Holland, Hong Kong, Hungary, Iceland, India, Israel, Italy, Japan, Jordan, Korea, Lebanon, Mexico, Netherlands, New Zealand, Norway, Panama, Poland, Portugal, Russia, Singapore, South Africa, Spain, Sweden, Switzerland, Taiwan, Turkey, United Kingdom, Uruguay, and Venezuela. The Zilver® Vascular Stent has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

VIII. Adverse Events

A. Observed Adverse Events/Complications

Following completion of a 20 patient pilot study, 151 patients were enrolled in a pivotal study at 24 U.S. investigative sites to evaluate the safety and effectiveness of the Zilver® Vascular Stent for use as an adjunct to percutaneous transluminal angioplasty (PTA) in the treatment of symptomatic vascular disease of the iliac arteries. Patients were eligible for enrollment if they had stenotic or occlusive lesions of the external or common iliac arteries.

Of the twenty patients enrolled in the pilot study, one patient (5%) had a target lesion revascularization at 251 days post-procedure. No other major adverse events were reported in the pilot study out to nine months post-procedure.

Table 2 shows the adverse events and complications reported in the pivotal study. Events that occurred while the patients were hospitalized and cumulative events through 9 months post-implant are presented. There were a total of 8 deaths, 3 myocardial infarctions (MI), 1 target lesion revascularization, and 1 limb loss. (Note: Two patients experienced two events each as discussed below.)

Of the 11 patients with 13 MAE reportable events, only 4 were determined to be procedure or device related by the Clinical Events Committee (CEC). These included 1) a death due to ventricular fibrillation 4 hours post-procedure; 2) a death due to multi-system organ failure secondary to hypoperfusion 1 day post-procedure; 3) a MI 3 days post-procedure and subsequent death 8 days post-procedure; and 4) a clinically driven target lesion revascularization at 36 days.

The CEC determined that the Major Adverse Events (MAE) in the remaining 7 patients were not related to the stenting procedure, but were related to pre-existing conditions. These included 1) a death at 37 days due to end stage cardiomyopathy and acute to chronic renal failure; 2) a death at 44 days due to lung cancer; 3) a death at 76 days from respiratory failure due to chronic obstructive pulmonary disease (COPD) exacerbation and pulmonary fibrosis following discharge from a hospitalization for Methicillin-resistant Staphylococcus aureus (MRSA) pneumonia; 4) a non-Q-wave MI at 87 days followed by a below-knee amputation at 119 days due to a new distal lesion; 5) a non Q-wave MI at 49 days following an urgent coronary artery bypass graft (CABG) procedure on day 45; 6) a death at 189 days due to respiratory failure secondary to congestive heart failure; and 7) a death due to septicemia of an infected femoral-popliteal bypass graft and cardiopulmonary arrest at 197 days.

The highest incidence in-hospital events/complications included blood loss requiring transfusion (3.3%), death (2.6%) and pseudoaneurysm or arteriovenous (AV) fistula at the access site (2%). The highest incidence cumulative, post-implant events through 9 months included worsened claudication/rest pain (7.3%) and death (5.3%).

Table 2. Adverse Events/Complications Observed in Patients Implanted with the Zilver® Vascular Stent

Adverse Event/Complication	In-Hospital	Cumulative thru 9 Months
Death[1]	2.6% (4/151)	5.3% (8/151)
MI (Non-Q-Wave and Q-Wave)[1]	0.7% (1/151)	2.0% (3/151)
Total Lesion Revascularization	0.0% (0/151)	0.7% (1/151)
Limb Loss[1]	0.0% (0/151)	0.7% (1/151)
Arterial Aneurysm/Rupture	0.0%(0/151)	0.0%(0/151)
Blood Loss Requiring Transfusion	3.3%(5/151)	4.6%(7/151)
Blue Toe Syndrome	0.0%(0/151)	0.7%(1/151)
Drug/Allergic Reactions Requiring Antibiotics	0.7%(1/151)	0.7%(1/151)
Embolism	0.0%(0/151)	0.0%(0/151)
Hematoma at Access Site Requiring Intervention	1.3%(2/151)	1.3%(2/151)
Hemorrhagic Stroke with Deficit	0.0%(0/151)	0.0%(0/151)
Iliac Artery Spasm	0.0%(0/151)	0.0%(0/151)
Iliofemoral Bypass Graft Surgery	0.0%(0/151)	1.3%(2/151)
Infection/Abscess Formation	0.0%(0/151)	3.3%(5/151)
Pseudoaneurysm or AV Fistula at the Access Site	2.0%(3/151)	3.3%(5/151)
Thrombosis of Culprit Lesion	0.0%(0/151)	0.7%(1/151)
Tissue Necrosis Requiring Debridement	0.7%(1/151)	4.0%(6/151)
Worsened Claudication/Rest Pain	0.7%(1/151)	7.3%(11/151)

[1] Two patients experienced multiple major adverse events. One patient had a non-Q-wave MI on day 87 followed by a limb loss on day 119; and another had an MI on day 3 followed by death on day 8.

B. Potential Adverse Events

Adverse events that may occur following Zilver® Vascular Stent implantation include, but are not limited to, the following:

- Abrupt stent closure
- Allergic reaction to nitinol
- Amputation
- Angina/coronary ischemia
- Arrhythmia
- Arterial aneurysm
- Arterial rupture
- Arteriovenous fistula
- Atheroembolization (Blue Toe Syndrome)
- Death
- Embolism
- Fever
- Hematoma/hemorrhage
- Hypersensitivity reactions
- Hypotension/hypertension
- Infection/abscess formation at access site
- Intimal injury/dissection
- Ischemia requiring intervention (bypass or amputation of toe, foot, or leg)
- Myocardial infarction
- Pseudoaneurysm formation
- Pulmonary embolism
- Renal Failure
- Restenosis of the stented artery
- Septicemia/bacterimia
- Stent malapposition
- Stent migration
- Stent strut fracture
- Stroke
- Spasm
- Tissue necrosis
- Worsened claudication/rest pain

C. Observed Device Malfunctions

No device malfunctions were reported during this study.

IX. Summary of Non-Clinical Laboratory Studies

A. Biocompatibility Testing, Packaging and Sterilization

Biocompatibility Testing

Biocompatibility of the Zilver® Vascular Stent and delivery systems was demonstrated by testing a device that was sufficiently similar to the Zilver Vascular Stent and delivery system with respect to the biocompatibility testing. The following tests were conducted with acceptable results:

- Rat subchronic intravenous toxicity
- *In vitro* hemolysis
- Cytotoxicity
- 2- and 12-week muscle implantation
- C3A Complement Activation
- Plasma Recalcification
- Mouse systemic toxicity
- Rabbit intracutaneous reactivity
- Genotoxicity (reverse mutation and chromosomal aberration)
- Guinea pig maximization sensitization
- Thromboresistance in dogs
- Mouse bone marrow micronucleus
- Material-mediated pyrogenicity

Packaging

The Zilver® Vascular Stent and delivery system are packaged within a protective holder, placed in a tray, and sealed within a Tyvek/polyethylene outer pouch. Burst pressure, permeability, and peel testing was conducted on packages containing non-aged devices, three-year accelerated aged devices, and real-time aged devices to evaluate package integrity following a shipping and distribution simulation. Test results demonstrate that the package design for the Zilver® Vascular Stent and delivery system is adequate for use in a typical shipping and distribution environment following a three-year shelf-life.

Sterilization

The Zilver® Vascular Stent and delivery system are sterilized using an ethylene oxide gas cycle in accordance with the methods described in the Medical Devices-Validation and Routine Control of Ethylene Oxide Sterilization, ANSI/AAMI/ISO-11135-2002 standard. Validation results demonstrated that the sterilization process can achieve a sterility assurance level of 10^{-6} and that residual levels were within acceptable ranges.

B. Bench Testing (including Shelf Life Testing)

Table 3 presents the assessments made during a series of non-clinical laboratory studies as well as the acceptance criteria (if applicable) and the results of the assessments. All of the test results met the predetermined acceptance criteria.

Table 3. Summary of Bench Testing Performed on the Zilver® Vascular Stent

Assessment	Purpose/Acceptance Criteria	Pass/No Pass or Result
Full Chemical Analysis	Characterization Only	54.5%-57.0% Nickel, Balance Titanium
Austenite Finish Temperature of Nitinol	Characterization Only	25 ± 4 °C
Mechanical Properties of Nitinol Cannula	Characterization Only	Ultimate tensile strength (UTS) = 1000 MPa, Total Elongation = 10%, Loading Plateau Stress = 460 MPa, Unloading Plateau Stress = 150 MPa
Post-Processing Mechanical Properties	Characterization Only	UTS = 1333 MPa
Corrosion	Characterization Only	Corrosion rate < 0.02 mm/year
MRI Compatibility at 1.5 and 3 Tesla	ASTM F2503-05 for deflection, characterization only for temperature rise, torque, and image artifacts	Acceptable for Clinical Use
Covered Surface Area (%)	Characterization Only	5 Fr-9.1% to 22.8% 6 Fr -11.2% to 22.8% 7 Fr-11.5% to 19.9%
Unconstrained Stent Diameter	± 0.7 mm of nominal diameter on average	Pass
Uniformity of Stent Diameter	< 5% difference in orthogonal diameters	Pass
Uniformity of Diameter Along Stent Length	< 5% variation in smallest and largest diameter	Pass
Unconstrained Stent Length	+ 2 mm / -5 mm of nominal length on average	Pass
% Change in Stent Length	< 25% between pre-deployment and unconstrained length	Pass
Stent Integrity	No microscopic evidence of structural deficiency at 50-63X	Pass
Deployment System Diameter	≤ 1.83 mm on average for the 5 Fr, ≤ 2.108 mm on average for the 6 Fr, ≤ 2.41 mm on average for the 7 Fr	Pass
Radiopacity	Adequate visualization under fluoroscopy	Pass
Radial Force	5 Fr and 6 Fr (1.3)- 0.028 N/mm ≤ X ≤ 0.56 N/mm at 1 mm less than the nominal stent diameter, 6 Fr (1.6) and 7 Fr- 0.04 N/mm ≤ X ≤ 0.8 N/mm at 1 mm less than the nominal stent diameters	Pass
Finite Element Analysis	Safety factor greater than 1	Pass
In Vitro Pulsatile Fatigue (Non-Overlapping State)	After 400 million cycles, stent remains one connected structure.	Pass
In Vitro Pulsatile Fatigue (Overlapping State)	After 400 million cycles, stent remains one connected structure.	Pass
Tensile Testing of Delivery	Average tensile strength > 15 N, no single	Pass

System	test article under 10 N	
Tip Bend Testing of Delivery System	Characterization Only	The kink radius of all sizes of the delivery systems was 10 mm.
Torque Testing of Delivery System	Characterization Only	Pass

A three year shelf life has been substantiated for the Zilver® Vascular Stent. Product function and specifications were demonstrated after three years of accelerated aging testing.

C. Animal Testing

One-month and six-month porcine studies (nine swine per time point) involving single stents and one-month and three-month porcine studies (five swine per time point) involving overlapping stents were conducted to assess the performance and functional biocompatibility of the Zilver® Vascular Stent and delivery system. Single stents were implanted in carotid arteries and aortas and overlapping stents were implanted in iliofemoral arteries. Angiography, quantitative histomorphometry, histopathology, and necropsy were performed. In addition, an evaluation of the Zilver® Vascular Stent integrity was performed.

All Zilver® Vascular Stents were successfully implanted and remained structurally intact for the duration of implantation. Following implantation, the vessels exhibited minimal late loss and diameter stenosis according to angiography. Quantitative histomorphometry showed minimal neointimal thickness and area stenosis. The vessels showed minimal injury and inflammation and were completely endothelialized according to the histopathologic evaluation. In addition, there was no evidence of thrombus or fibrin deposition. Gross examination of the body systems of the swine revealed no changes/lesions associated with the single or overlapping Zilver® Vascular Stent.

X. Summary of Clinical Investigations

A pilot study of the safety of the Zilver® Vascular Stent enrolled 20 patients at four investigative sites and provided justification for initiation of a pivotal study to assess the safety and effectiveness of the Zilver® Vascular Stent.

A total of 151 patients at 24 U.S. investigative sites were enrolled in a pivotal study to evaluate the safety and effectiveness of the Zilver® Vascular Stent for use as an adjunct to percutaneous transluminal angioplasty (PTA) in the treatment of symptomatic vascular disease of the iliac arteries. The following is a summary of the pivotal study.

Study Endpoints:

This prospective , non-randomized study of the Zilver® Vascular Stent for the treatment of stenotic or occlusive lesions of the external or common iliac arteries was intended to establish the rate of major adverse events (MAE) at nine-month clinical follow-up as the primary study endpoint compared to an Objective Performance Criterion (OPC) derived from literature of recent studies in similar patient populations. The MAE rate of the OPC was set to be not greater than 16%, with a 9% delta. Secondary endpoints included acute procedure success, 30-day clinical success, nine-month patency rate based on ultrasound examination, ankle-brachial index (ABI), and nine-month functional status as measured by the walking impairment questionnaire.

Patient Population:

Patients eligible to enroll in this study had up to two documented stenotic (≤10 cm long) or occluded (≤5 cm long) atherosclerotic lesions of the external iliac or common iliac artery on opposite sides. Lesions could be either *de novo* or restenotic. Patients with previously stented lesions were excluded. Characteristics of the patients enrolled in this study including age, gender, medical history as well as angiographic characteristics of the treated lesions (pre-procedure) are included in Tables 4 and 5.

Table 4. Characteristics of Patients Implanted with the Zilver® Vascular Stent

Baseline Characteristics		N=151 Patients	
Age (Mean years +/- SD)		67 ± 8.9	
Male Gender		93	61.6 %
Smoking Status	Past	79	52.3%
	Current	65	43.0%
Diabetes		46	30.5%
Hypercholesterolemia		109	72.2%
Hypertension		117	77.5%
Carotid Disease		49	32.5%
Renal Disease		23	15.2%
Pulmonary Disease		50	33.1%
Use of antiplatelets		116	76.8%
Congestive Heart Failure (CHF) Class 3 or 4		7	4.6%
Previous MI		47	31.1%

Table 5. Angiographic Characteristics of Lesions Prior to Treatment with the Zilver® Vascular Stent

Angiographic Characteristics	Lesions (n=177)	Mean ± S.D.
Lesion Length (mm)	168	32.9 ± 18.8
Reference Vessel Diameter (RVD) (mm)	171	7.4 ± 1.5
In-Stent Minimum Lesion Diameter (MLD) (mm)	171	2.7 ± 1.4
% Diameter In-Stent Stenosis	171	64.5 ± 15.2

Methods:

All patients underwent PTA (predilatation) of the target lesion prior to deployment of the stent. Up to two lesions/patient on opposite sides were stented with no more than two stents/lesion. Patients had an angiogram prior to and immediately following stent placement. Duplex ultrasound to assess patency of the stented artery and common femoral artery was performed no more than three days following the procedure. The protocol recommended each hospital follow their standard protocol with respect to pre- and post-procedure medication; based on previous published studies clopidogrel was suggested before and post procedure for 6 months. Patients underwent clinical follow-up at 1 and 9 months post-procedure. Clinical follow-up at 1 month included measurement of ABI on the treated side as well as completion of a walking impairment questionnaire. Follow-up at 9 months included measurement of ABI on the treated side as well as completion of the walking impairment questionnaire, and ultrasound to evaluate patency. In addition, patients were contacted by telephone at 6 months post-procedure. All data were recorded on case report forms at the investigative sites. Core laboratories analyzed angiographic and ultrasonic imaging.

Results:

The primary study endpoint is the MAE rate occurring within nine months post-procedure. MAEs include death, MI (non-Q-wave and Q-wave), target lesion revascularization, and limb loss on the same side as the treated lesion. Success of the study required that the MAE rate be less than or equal to a predetermined OPC of 16%. All MAEs were also adjudicated with respect to their relationship to the study device and procedure by an independent CEC.

Table 6 presents the MAEs that occurred within 9 months of device placement. (Note: For patients with an MI who experienced a subsequent event within nine months of device placement, the worst event is counted and presented in the table.) All patients

have completed their 9-month follow-up or reached a study endpoint. Five (5) of the 151 patients (3.3%) have been confirmed as withdrawn or lost to follow-up. Therefore, there were 146 evaluable patients available for assessment of MAE within the entire 9-month follow-up period. This number (146) exceeds the sample size of 130 patients determined *a priori* to be necessary to provide at least 80% power for this measure. Rates for CEC-adjudicated related events as well as total events are shown in Table 6. Of primary interest is the MAE rate at 9 months post-procedure for events adjudicated by the CEC as related to the device or the procedure. This rate is 2.7% (4/146). For related and non-related events combined, the total MAE rate is 7.5% (11/146). These study results demonstrate that the MAE rate of the Zilver® Vascular Stent is not greater than the target value of 16%.

Table 6. Summary of Protocol Defined Major Adverse Events Observed in 146 Patients Implanted with the Zilver® Vascular Stent

Major Adverse Event	Related Events (CEC Adjudicated)		All Events	
	N	%	N	%
Death [1]	3	2.0	8	5.5
MI (Non-Q-Wave and Q-Wave)	0	0.0	1	0.7
TLR	1	0.7	1	0.7
Limb Loss [2]	0	0.0	1	0.7
Total	4	2.7	11	7.5

[1] One patient experienced a MI 5 days prior to the death.

[2] One patient experienced a non-Q-wave MI 32 days prior to the limb loss.

Table 7 focuses on all (related and non-related) observed major adverse events and demonstrates that for evaluable patients (n=146), the MAE rate is 7.5% (11 of 146). A more conservative analysis of all evaluable patients counts all patients who withdrew from the study and all who were lost to follow-up as Major Adverse Events. In this conservative approach, the MAE rate becomes 10.6% (16 of 151). By both methods of analysis, the MAE point estimate rate is well below the OPC target value of 16%. This indicates that the primary study endpoint was met.

Table 7. Rates for All Major Adverse Events within 9 months post-procedure

	Pivotal Study Result		OPC	
	Point Estimate	2-sided 95% CI Upper Bound	Target Value	Upper Limit
All enrolled patients [1]	16/151 (10.6%)	16.6%	16%	25%
Evaluable patients [2]	11/146 (7.5%)	13.1%		

[1] 5 patients who could not be assessed at 9 months (i.e., 1 withdrawn and 4 lost to follow-up) were imputed as experiencing MAE as a worst case analysis that may over-estimate actual rates.

[2] Major adverse events in 7 of the 11 patients reported with MAE were adjudicated by an independent Clinical Events Committee as not related to the device or the procedure.

Effectiveness of the Zilver® Vascular Stent was confirmed by clinical and imaging assessment post-procedure and at follow-up time points. Effectiveness measures included acute procedure success, thirty-day clinical success, ankle-brachial index, patency, and nine-month functional status measured by the walking impairment questionnaire. These measures are summarized in Table 8.

Table 8. Effectiveness Measures for Patients Implanted with the Zilver® Vascular Stent

Effectiveness Measure	Pre-Procedure	Post-Procedure	One-Month	Nine-Month
Acute Procedure Success		93.3% (140/150)[1]		
30-day Clinical Success			94.0% (141/150)	
ABI[2]	0.68 ± 0.23 (N=154)	0.88 ± 0.29 (N=152)	0.86 ± 0.20 (N=140)	0.87 ± 0.21 (N=137)
Patency of Stented Lesion		99.2% (123/124)		92.9% (105/113)
Walking Distance Score	20.1 ± 28.8 (N=147)		63.5 ± 38.3 (N=138)	55.8 ± 40.1 (N=124)
Walking Speed Score	25.6 ± 29.2 (N=141)		63.1 ± 37.4 (N=131)	56.7 ± 37.5 (N=119)

[1] One patient was excluded from the analysis due to placement of a non-study stent during the procedure.
[2] There were 177 treated lesions in the study that occurred in 170 limbs. N = number of limbs treated.

Acute procedure success was defined in the protocol as "vessel with <30% residual stenosis determined angiographically immediately after stent placement and no major clinical events before discharge." Furthermore, patients with multiple treated vessels are considered to be acute procedure failures if any of their treated vessels are ≥ 30% stenosed. The acute procedure success was 93.3% for the pivotal study. Ten patients experienced acute procedure failure. Six of the 10 failures had ≥ 30% residual stenosis, and the remaining 4 patients experienced major adverse events (3 deaths and 1 MI) prior to hospital discharge. Two of the three deaths, and the MI, were adjudicated as procedure-related by the Clinical Events Committee.

Thirty-day clinical success was defined in the protocol as "vessel with <30% residual stenosis immediately after stent placement and no major clinical events within 30 days of implant." Thirty-day clinical success was 94.0% for the pivotal study. Nine patients out of the ten patients that were considered to be acute procedure failures were also thirty-day clinical failures.

ABIs were measured pre-procedure, post-procedure, and at one- and nine-month follow-up. ABI was seen to improve from pre- to post-procedure, as well as from pre-procedure to one-month and nine-month follow-ups. After the procedure, ABI was little changed at

one-month follow-up and nine-month follow-up relative to the post-procedure value. These findings suggest that the improvement achieved immediately after stent placement is maintained up to nine months post-procedure.

Ultrasound was performed no more than three days post-procedure and at nine-month follow-up to assess treated vessel patency within the stented region. Patency rates were high both post-procedure and at the nine-month follow-up (99.2% and 92.9%, respectively). Imaging was not performed, or was inadequate for assessment, for 53 lesions immediately post-procedure and for 52 lesions at follow-up.

The Walking Impairment Questionnaire is a measure of patient-perceived walking performance for patients with peripheral arterial disease (PAD) and/or intermittent claudication. Distance and speed scores are calculated by expressing each patient's score as a percentage of the maximum score possible, with higher scores indicating a patient's perception of greater walking distance and/or speed. Table 8 presents the walking distance and speed scores pre-procedure, at one-month follow-up, and nine-month follow-up. The walking distance and speed both increased from pre-procedure to one-month follow-up, and from pre-procedure to nine-month follow-up. From one- to nine-month follow-up there is a slight decrease in both scores. These decreases may be due to progression of the disease rather than directly related to stent performance. More importantly, walking distance and speed at 9-month follow-up continues to be improved relative to pre-procedure values.

Sub-analysis of patients with overlapping stents:

According to the study protocol, patients were eligible to receive up to two stents per lesion. As a result, some patients received overlapping stents to treat a single lesion. Twenty-four patients (15.9%) received at least one pair of overlapping stents. Comparisons were made between results from patients with non-overlapping stents and patients with overlapping stents. Patients with overlapping stents were slightly older with a greater proportion of males. Although patients with overlapping stents had a lower incidence of diabetes, they had a greater incidence of high cholesterol, hypertension, and carotid, renal, and pulmonary disease. Of the 11 major adverse events that occurred within nine months post-procedure, four of the events occurred in patients with overlapping stents. However, according to the CEC, none of these four events were iliac repair related. Acute procedure success rate and 30-day clinical success were 87.5% and 91.7%, respectively, for patients with overlapping stents. Trends in ABIs were similar to patients with non-overlapping stents, showing a significant increase in ABI pre-procedure to post-procedure and maintenance of ABI post-procedure to nine-month follow-up.

Treated vessel patency was high for patients with overlapping stents post-procedure and at nine-month follow-up (100% and 82.4%, respectively). Of those patients with overlapping stents, imaging was not performed, or was inadequate for assessment, for 13 lesions immediately post-procedure and for 11 lesions at follow-up. Walking impairment scores including distance and speed improved for patients with overlapping stents from pre-procedure to one-month follow-up and pre-procedure to nine-month follow-up. From one- to nine-month follow-up time points, patients with overlapped stents had no significant changes in their walking distance and speed scores. In summary, despite more prevalent comorbid conditions, effectiveness measures such as acute procedure success, 30-day clinical success, ABIs, patency, and walking distance and speed scores were improved for patients with overlapping stents. These measures are summarized in Table 9.

Table 9. Effectiveness Measures for Patients Implanted with overlapping Zilver® Vascular Stents

Effectiveness Measure	Pre-Procedure	Post-Procedure	One-Month	Nine-Month
Acute Procedure Success		87.5% (21/24)		
30-day Clinical Success			91.7% (22/24)	
ABI[1]	0.65 ± 0.24 (N=24)	0.84 ± 0.28 (N=23)	0.86 ± 0.26 (N=23)	0.80 ± 0.24 (N=18)
Patency of Stented Lesion		100% (20/20)		82.4% (14/17)
Walking Distance Score	20.7 ± 30.7 (N=24)		53.5 ± 43.3 (N=24)	52.8 ± 40.0 (N=17)
Walking Speed Score	17.2 ± 25.0 (N=20)		55.9 ± 44.3 (N=22)	48.3 ± 42.8 (N=16)

[1] N = number of limbs treated.

XI. Conclusions from Non-Clinical and Clinical Investigations

Based on the results of bench and animal studies, the Zilver® Vascular Stent meets or exceeds safety and performance specifications.

Results of the pivotal clinical study provide a reasonable basis for determining the safety and effectiveness of the Zilver® Vascular Stent as an adjunct to percutaneous transluminal angioplasty in the treatment of symptomatic vascular disease of the iliac arteries. The pivotal study showed a device or procedure related major adverse event rate at nine months post-procedure to be 2.7%, which is below the objective performance criterion (OPC) of 16% designated for the study. Furthermore, the total major adverse event rate was 7.5%, also below the OPC. Effectiveness measures such as acute

procedure success, patency, and improvements in ABIs, and walking distance and speed scores over time were also acceptable. Finally, analysis of patients receiving overlapping stents did not raise any device safety or effectiveness concerns.

XII. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH Decision

FDA issues an approval order on June 26, 2006.

The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

XIV. Approval Specifications

Instructions for Use: See labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.